STUDIES ON FLUID METABOLISM IN ESSENTIAL FATTY ACID DEFICIENCY

KOBAYASHI, MASAO

原　　著

STUDIES ON FLUID METABOLISM IN ESSENTIAL FATTY ACID DEFICIENCY

by

MASAO KOBAYASHI

From the 2nd Surgical Division, Kyoto University Medical School
(Director: Prof. Dr. YASUMASA AOYAGI)

Received for publication Mar. 9, 1961

I. INTRODUCTION

The concept, "Milieu interieur," first brought modern medicine to the recognition of the significance of body fluid. CLAUDE BERNARD[1] showed that the real medium in which the organism lives is not the external environment but internal environment, which is composed of the organic fluid of the circulating blood and the interstitial fluid that bathes every cellular element in all tissues. So, the maintenance of constancy in this internal environment is the first condition necessary for maintaining equilibrium and independence of life. CANON[2] gave the word "Mechanism of Homeostasis" to the physiological co-operative mechanism which maintains this healthy internal environment.

From the carefully detailed basic investigative studies of the laboratory of Dr. FRANCIS D. MOORE[3)4] have come the interpretations and formulations of the normal and abnormal responses to injury.

The organism is composed of tissue cells, and recently it has become gradually recognized that the basic constituent element of tissue cells is lipoprotein rather than simple protein. Therefore, enough fat of good quality has to be supplied in addition to protein to provide a perfect supply of nutrients in surgical cases in which the primary object is the repair and reconstruction of tissues. Fat is no longer significant as a caloric source only, but it also plays an important role in the fulfilment of living functions and the construction of tissues. It is, therefore, supposed that a supply of fat in surgical cases is also necessary to maintain the constancy of fluid distribution in the body as much as possible.

Research workers in our laboratory had noticed this important role of fat, and succeeded in manufacturing a 20% sesame oil emulsion after several years' efforts to obtain a fat emulsion which could be infused intravenously. It has already been demonstrated clinically by them[5)~13] that pre- and postoperative infusions of this emulsion were very effective. KUYAMA[14] and HANAFUSA[15] in our laboratory observed that when this emulsion was repeatedly infused intravenously before and after operation, it caused a remarkable economization of protein and storage fat, and, therefore, it could prevent postoperative complications, and the patients could recover sooner from surgery. This effect was believed to be brought about not only because the sesame oil emulsion was utilized as a caloric source in the body, but also because the essential fatty acids (abbreviated as EFA) such as linoleic and linolenic acids which were contained abundantly in the emulsion, worked as constant elements and accelerated the repair of tissues and the recovery of the living function. Nagase[16] in our laboratory has demonstrated that EFA-deficiency induced an increased permeability of the capillaries and cell membranes and decreased the adrenocortical capacity, and that the EFA-deficient animal easily developed water intoxication and acute postoperative pulmonary edema following postoperative overhydration. Tamaki[17] in our laboratory observed that the administration of the sesame oil emulsion to patients before and after gastrectomy maintained the serum colloidal osmotic pressure and extracellular water volume at near the normal level from the clinical view-point.

The author administered repeatedly the sesame oil emulsion both pre- and postoperatively to gastrectomy dogs and studied experimentally the fluid distribution in order to investigate again in detail Tamaki's experiment[17].

II. EFFECTS OF INTRAVENOUS INFUSION OF THE FAT EMULSION ON BODY FLUID DISTRIBUTION BEFORE AND AFTER GASTRECTOMY IN HEALTHY ADULT DOGS

A. MATERIALS

(1) Fat Emulsion and the Method of Infusion

As mentioned above, 20% sesame oil emulsion was used. This emulsion contained 7% glucose and was rich in EFA, too.

In dehydration experiments, 2cc per kg of body weight of this emulsion was diluted by 10cc per kg of body weight of balanced electrolyte solution (abbreviated as BES), 10 cc per kg of body weight of 5% glucose solution, 5mg of vitamin B_1, 25mg of vitamin B_2 and 100 mg of vitamin C. And it was infused intravenously repeatedly by syringe once a day during the preoperative 5 days and the postoperative 10 days. Potassium was added to the diets.

In overhydration experiments, 2cc per kg of body weight of this emulsion was diluted by 10cc per kg of body weight of Ringer's solution, 10cc per kg of body weight of 5% glucose solution, 5mg of vitamin B_1, 25mg of vitamin B_2 and 100mg of vitamin C during the preoperative 5 days. During the postoperative 4 days (0~+3), the same volume of the emulsion was given as 40cc per kg of body weight of Ringer's solution, 40cc per kg of body weight of 5% glucose solution and the same vitamins, and during the following postoperative 7 days (+4~+10) the same volume of the emulsion was given as 30cc per kg of body weight of each solution and the same vitamins. And they were infused intravenously repeatedly by syringe once a day. But in these experiments, potassium was not added to the diets.

(2) Experimental Animals

Healthy adult male dogs, which had a body weight of about 10kg, were employed for this study, and they were divided into two groups: the first group was infused with fat emulsion as the fat group, the second group was not infused with the emulsion as the control group. The experimental dogs were fed during the preoperative 10 days and postoperative 15 days in the boxes which were provided with a collecting apparatus for urine. Gastrectomy (BILLROTH I.) was performed as the surgical procedure under intravenous anesthesia with 0.5cc per kg of body weight of 5% pentobarbital sodium solution. Urine was collected by the collecting apparatus for urine and catheterization was done with NELATON's catheter. On the 15th day after operation, the bilateral carotid arteries were cut across allowing the blood to flow freely. After the blood flow ceased, parts of various organs were dissected, and their water contents were measured by the dry weight method.

B. METHODS

(1) Measurement of Total Body Water Volume[18)19)20)]

50mg per kg of body weight of 2% solution of NAAP (N-acetyl 4-aminoantipyrine) was used as the reagent. NAAP disappears from the dog at a rate of about 20% per hour. Only about 60% of the NAAP administered to a dog can be accounted for in the urine, the remainder is metabolized. Only the extrapolation procedure, therefore, can be applied to the dog. In this experiment, total body water volume was calculated by the extrapolation procedure (Table 1 and Fig. 5).

(2) Measurement of Extracellular Water Volume[20)~30)]

Extracellular water volume was measured by SUNAHARA-CRANDALL-ANDERSON's method. 5% solution of Rhodansoda (Sodium thiocyanate) was used as the reagent.

(3) Calculation of Intracellular Water Volume

Intracellular water volume was determined by subtracting the extracellular water volume from the total body water volume.

(4) Measurement of the Circulating Plasma Volume[20)21)31)~37)]

Table 1. NAAP space in normal dogs.

Weight (kg)	Time after inject. of NAAP (hours)	NAAP injected (mgm)	Urine NAAP content (mgm)	NAAP retained (mgm)	Plasma NAAP conc. (mgm/l)	NAAP space (liters)	Extrapolation procedure
11.4	0	480					70mgm/l NAAP space =6.85l (60.0%)
	1		18.8	461.2	65.0	7.09	
	2		35.0	445.0	60.1	7.40	
	3		41.1	435.9	56.6	7.70	
	4		69.9	410.1	51.7	7.93	
	5		111.2	368.8	47.2	7.81	
	6		156.9	323.1	42.8	7.54	
9.5	0	460					61mgm/l NAAP space =7.54l (79.1%)
	3		136.8	323.2	36.6	8.9	
	4½		167.7	292.3	28.6	10.2	
	6		202.2	257.8	22.1	11.5	

0.3% solution of Evansblue (T-1824) was used as the reagent.

(5) Calculation of the Circulating Blood Volume[20)21)31)~37)]

Circulating blood volume was determined by the following formula:

Circulating blood volume=

$$\frac{\text{Circulating plasma volume}}{100-\text{Ht. }(\%)}\times 100$$

(6) Measurement of the Hematocrit Value

The hematocrit value was measured by WINTROBE's method[13)].

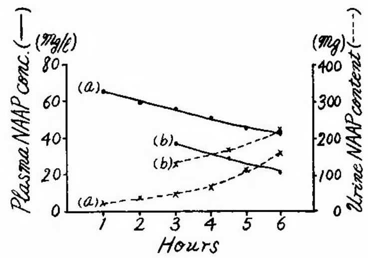


Fig. 5 Changing of plasma conc. and urinary excretion after NAAP inject. in normal dogs.

(7) Calculation of the Interstitial Water Volume

Interstitial water volume was determined by subtracting the circulating plasma volume from the extracellular water volume.

(8) Measurement of the Concentration of Serum Protein

Concentration of serum protein was measured with a refractometer[38)] manufactured by the HITACHI Industrial Co.

(9) Measurement of the Serum Colloidal Osmotic Pressure[39)~42)]

Serum colloidal osmotic pressure was measured by KROGH-NAKAZAWA's first method[39)].

(10) Measurement of the Serum Protein Fraction

Serum protein fraction was measured by paper electrophoresis[13)].

(11) Water Balance

Primary water balance was decided by subtracting the volume of excretion, except for insensible water loss, from the volume of water intake.

(12) Water Content in Various Organs

As mentioned above, the surfaces of the organs dissected, as soon as the dogs were killed by cutting across the bilateral carotid arteries, were dried lightly on blotting paper before the organs were weighed. They were dried for 72 hours in a dessicator at 70°C, and their water contents were calculated by subtracting the dry weight from the wet weight of each.

C. RESULTS AND DISCUSSION[44)~47)]

(1) Total Body Water Volume (abbreviated as TBW)

In the fat group, TBW increased preoperatively in both the dehydration and overhydration experiments. On the other hand, in the control group, TBW decreased in both experiments.

In the dehydration experiments, TBW in both groups decreased after the postoperative 4th day, but in the fat group TBW showed a smaller decline than in the control group.

In the overhydration experiments, in the control group the TBW increased markedly after operation, but the TBW in the fat group showed a smaller increment than in the control group.

On the whole, in spite of dehydration and overhydration experiments, in the fat group TBW was maintained at nearer the normal level than in the control group throughout the pre- and postoperative stages (Table 2, Fig. 3 and Fig. 4).

This effect was believed to be brought about not only because the sesame oil emulsion was utilized as a caloric source in the body, but also because the essential fatty acids, working as constant elements in accelerating the repair of tissues and the recovery of physiological function, maintained effectively constancy of tissue cells, and thus caused a favorable influence on fluid metabolism in the body.

Table. 2 Comparison between fat group and control group in body weight, fluid distribution, hematocrit value, surum protein and serum colloidal osmotic pressure (Mean values).

Overhydration experiment

	Group	− 6	− 1	+ 4	+ 9	+ 14
Body weight (kg)	Fat	10.85	10.06	10.20	9.80	9.25
	Control	9.3	9.05	8.40	8.25	7.75
Total body water volume (l)	Fat	5.62	5.70	5.93	5.44	5.68
	Control	5.53	5.31	5.82	6.20	6.05
Extracellular water volume (cc)	Fat	2741	2715	3010	2869	2753
	Control	2563	1882	2878	3298	2916
Intracellular water volume (cc)	Fat	2876	2985	2910	2871	2927
	Control	2967	3488	2942	3002	3134
Circulating plasma volume (cc)	Fat	549	554	642	545	513
	Control	495	428	388	404	383
Circulating blood volume (cc)	Fat	831	827	931	778	789
	Control	917	751	617	621	598
Interstitial fluid volume (cc)	Fat	2195	2161	2368	2324	2240
	Control	2068	1394	2490	2894	2533
Hematocrit	Fat	34	33	31	30	35
	Control	46	43	40	35	36
Conc. of serum protein (g/dl)	Fat	7.2	7.1	6.9	7.1	7.2
	Control	6.8	6.4	6.0	5.8	6.5
Circulating serum protein (g)	Fat	39.5	39.3	41.3	38.6	37.0
	Control	33.6	27.4	23.3	23.4	24.9
Serum colloidal osmotic pressure (mmH_2O)	Fat	221	223	184	230	229
	Control	210	195	169	210	212

Dehydration experiment

	Group	− 6	− 1	+ 4	+ 9	+ 14
Body weight (kg)	Fat	14.90	15.05	14.15	14.15	13.5
	Control	10.35	10.20	9.30	9.30	9.10

Total body water volume (l)	Fat	10.68	11.25	10.23	10.12	9.34
	Control	6.41	6.34	5.92	5.63	5.42
Extracellular water volume (cc)	Fat	4222	3907	3561	3675	3318
	Control	2883	2240	2352	2372	2168
Intracellular water volume (cc)	Fat	6458	7343	6669	6445	6022
	Control	3527	4100	3568	3258	3252
Circulating plasma volume (cc)	Fat	603	619	771	582	544
	Control	493	483	469	484	423
Circulating blood volume (cc)	Fat	1005	967	1128	924	954
	Control	967	805	721	682	613
Interstitial fluid volume (cc)	Fat	3619	3288	2790	3092	2774
	Control	2390	1757	1883	1888	1745
Hematocrit	Fat	40	36	32	37	43
	Control	49	40	35	29	31
Conc. of serum protein (g/dl)	Fat	8.0	7.7	7.4	7.5	8.0
	Control	6.5	6.2	5.5	5.0	6.0
Circulating serum protein (g)	Fat	48.3	47.6	57.0	43.7	43.5
	Control	32.0	30.0	25.8	24.2	25.4
Serum colloidal osmotic pressure (mmH_2O)	Fat	335	304	279	326	327
	Control	291	196	232	196	239

Fig. 1 Dehydration experiments in normal dogs.

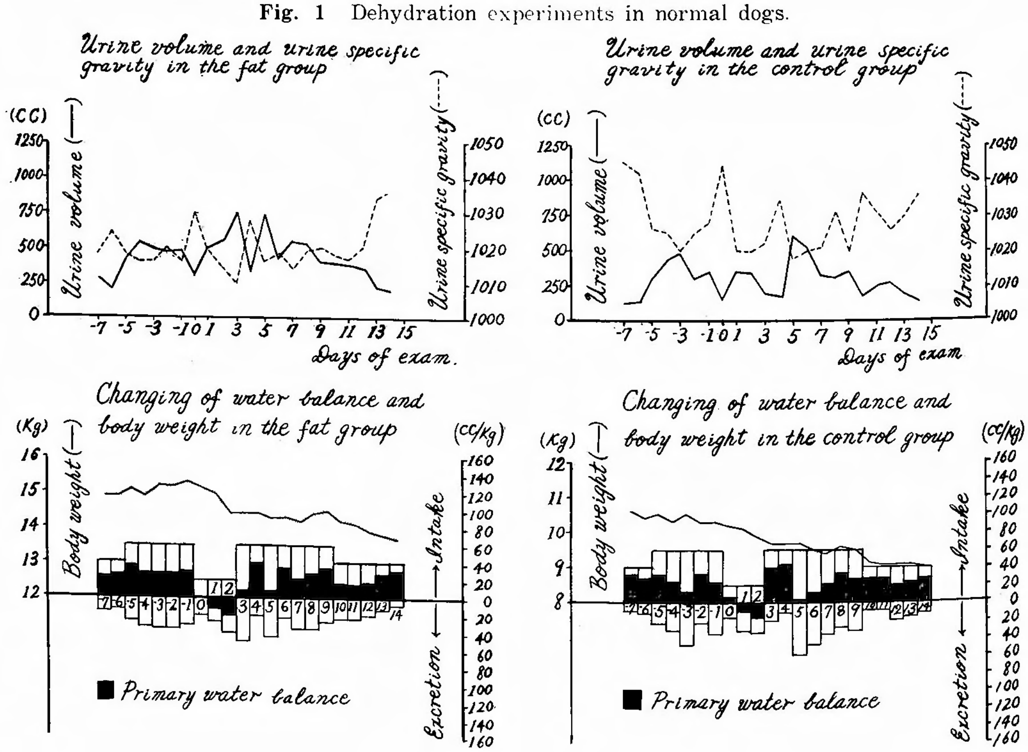


Fig. 2 Overhydration experiments in normal dogs.

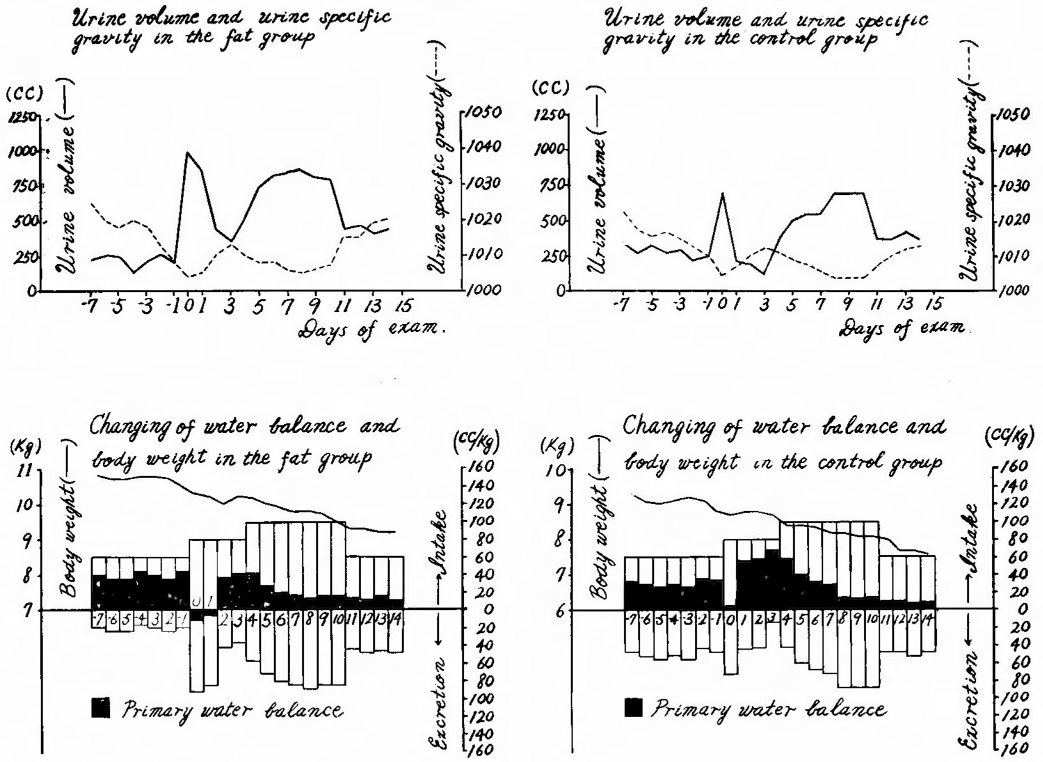


Fig. 3 Dehydration experiments in normal dogs.
(Changes in fluid distribution)

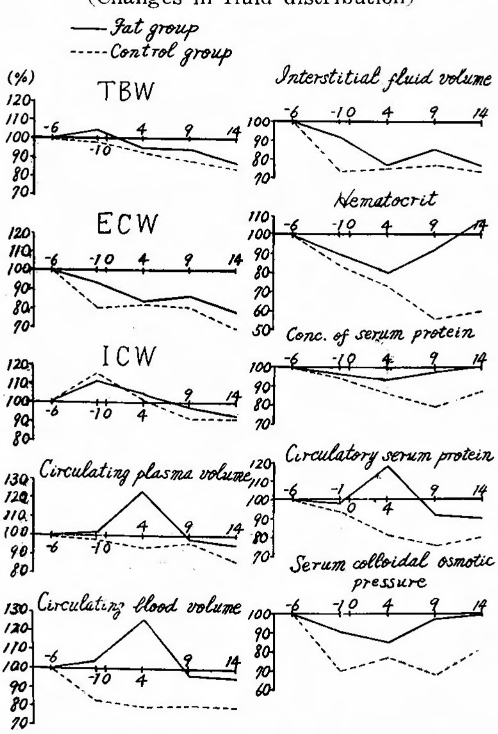
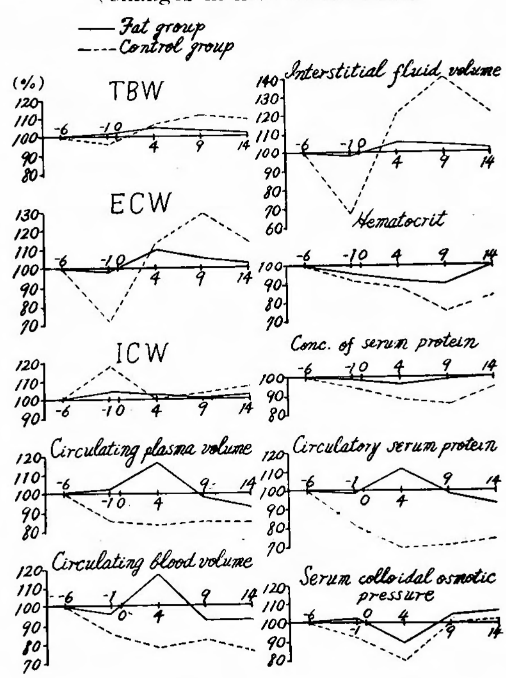


Fig. 4 Overhydration experiments in normal dogs.
(Changes in fluid distribution)



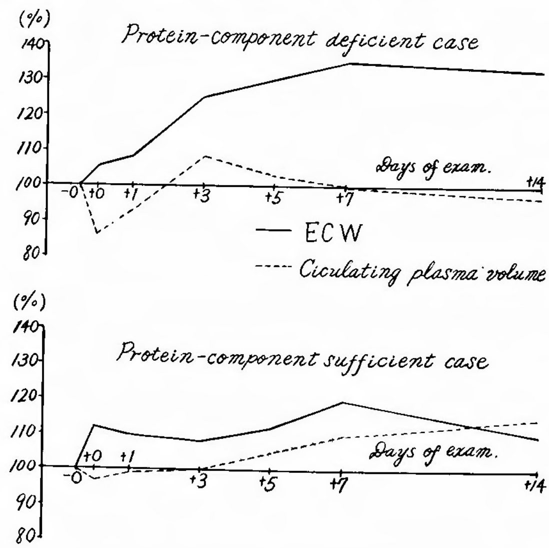
(2) Extracellular Water Volume (abbreviated as ECW)

In the fat group, in both the dehydration and overhydration experiments, changes in the ECW were less than in the control group.

Before operation in the fat group, ECW decreased slightly in the dehydration experiments, ECW increased slightly in the overhydration experiments. On the other hand, before operation in the control group, in both experiments ECW decreased more markedly than in the fat group (Table 2, Fig. 3 and Fig. 4).

The author compared the overhydration cases in which the administration of the fat emulsion was continually repeated throughout the pre- and postoperative stages with the overhydration cases in which the administration of protein-component sufficient solutions was done (Fig. 6).

Fig. 6 Changes in ECW and circulating plasma volume.



When the administration of the protein-component sufficient solutions such as whole blood, plasma and amino acid solutions was done, ECW increased slightly in spite of postoperative overhydration. Its expansion was only 10% at most. On the other hand, when the protein-component deficient solutions were given, ECW expanded remarkably following postoperative overhydration. Its expansion reached 30%, and in the latter, the increment of circulating plasma volume was delayed and was initiated after ECW had expanded. On the other hand, in the former it was caused in parallel with the ECW.

Therefore, it is understood that the administration of protein-component sufficient solutions continued pre- and postoperatively is necessary to keep body fluid stable. As shown in Fig. 4, in our overhydration experiments, it is also understood that the administration of the sesame oil emulsion throughout the pre- and postoperative stages together with electrolyte solution is very effective in maintaining ECW stably.

How closely ECW (Rhodan space) corresponds to the true extracellular water volume is still undetermined. However, in the view of the fact that permeability of the capillaries and cell membranes increases more abnormally in the control group than in the fat group, we can not neglect the possibility that certain amounts of thiocyanate probably enter the cells and the expansion of sodium thiocyanate space occurs more markedly in the control group than in the fat group.

(3) Intracellular Water Volume (abbreviated as ICW)

As shown in Table 2, Fig. 3 and Fig. 4, changes in ICW were slighter than in ECW. The changes in the fat group had more stability than in the control group.

(4) Circulating Plasma Volume and Circulating Blood Volume (Table 2, Fig. 3 and Fig. 4)

They showed normal values before operation in the fat group in both the overhydration and dehydration experiments. On the other hand, in the control group they decreased preoperatively in both experiments.

They increased postoperatively in the fat group not only in the overhydration experiments, but also in the dehydration experiments. This finding suggests that the administration of the emulsion did not induce a postoperative shocklike state. On the other hand, in the control group, they decreased postoperatively in both experiments and postoperative shocklike state was induced. As shown in Fig. 4, extravasation and pooling of body water into the interstitial space resulted in a marked degree after operation in the overhydration experiments of the control group.

The causes which induced such a remarkably abnormal state on the fluid distribution in the body in the control group were considered as follows: (1) As mentioned below, a fall in the serum colloidal osmotic pressure was induced markedly after operation in the control group. (2) In addition, an increased capillary permeability was caused markedly after operation in the control group.

It was demonstrated that postoperatively an effective circulating blood volume was not maintained in the control group, and that, on the other hand, it was maintained satisfactorily in the fat group. If the best working definition of shock is "a condition in which the volume of the circulating blood is too small in proportion to the capacity of the vascular bed"[15], the administration of the sesame oil emulsion before and after operation is very effective in order to prevent postoperative shock.

(5) Hematocrit Value (abbreviated as Ht.)

As shown in Fig. 3 and Fig. 4, the postoperative course of the Ht. was more favorable in the fat group in comparison with the control group.

(6) Concentration of Serum Protein, Electrophoretic Fraction and Total Circulating Serum Protein

As shown in Fig. 3, Fig. 4, Table 2 and Table 4, these experimental results were more favorable in the fat group in comparison with the control group throughout all the periods of these experiments.

The intravenously infused fat was first phagocytized by alveolar phagocytes, stellate cells of the liver and reticuloendothelial cells of the spleen in the form of O-lipoprotein. Then it was changed from glyceride into phospholipid in these cells,

Table. 4 Comparison between fat group and control group in concentration of serum protein, electrophoretic fraction and A/G (mean values).

Group	Days of examination	Conc. of serum protein (g/dl)	Serum protein: Electrophoretic fraction (%) Alb.	α-glob.	β-glob.	γ-glob.	Ratio A/G
Fat	−6	6.6	32.6	16.5	33.9	17.0	0.483
	−1	6.0	32.2	19.7	34.7	13.4	0.479
	+4	6.0	29.5	20.1	32.6	17.8	0.420
	+9	6.2	27.8	22.1	34.5	15.6	0.383
	+14	6.7	28.8	23.5	33.4	14.3	0.410
Control	−6	7.0	31.6	20.5	36.4	11.5	0.449
	−1	6.7	26.4	27.4	37.6	8.6	0.360
	+4	5.7	25.9	23.0	33.7	17.4	0.356
	+9	5.2	24.4	24.2	36.9	14.5	0.325
	+14	5.6	26.7	25.1	35.0	13.2	0.365

and finally transmitted into tissue cells of the whole body via the blood circulation in the form of α- and β-lipoprotein. And these were believed to be due to the smooth utilization of the infused fat emulsion throughout such process and to the economization of protein caused by the infusion of the fat emulsion[14)19)53)].

(7) Serum Colloidal Osmotic Pressure

As shown in Fig. 3, Fig. 4 and Table 2, the serum colloidal osmotic pressure was maintained much better in the fat group than in the control group throughout all the periods of these experiments.

The serum colloidal osmotic pressure can be calculated by the following formula:[44)]

$P = 5.5A + 1.4G$ mmHg

provided P : serum colloidal osmotic pressure

A : serum albumin concentration + serum α-globulin concentration

G : serum globulin concentration with exception of serum α-globulin concentration

The reasons why the administration of the emulsion was effective on the maintenance of the serum colloidal osmotic pressure could be considered as follows: (1) As shown in Table 4, the albumin concentration in serum was maintained higher in the fat group than in the control group throughout all the periods of these experiments. (2) As mentioned above, in the process of the fat metabolism in vivo α- and β- lipoproteins[51)52)] were produced. These lipoproteins had a favorable effect on the albumin, α- and β- globulin concentrations in the serum. (3) The administration of the emulsion induced a remarkable protein sparing action. Thus the repeated infusions of the fat emulsion inhibited a fall in the serum colloidal osmotic pressure for these reasons.

However, when changes in the fluid distribution in the body such as extracellular, intracellular, interstitial fluid and circulating plasma volume, are discussed, we should consider them not only from the view point of serum colloidal osmotic pressure as shown by STARLING's theory, but also from the standpoint of the permeability of capillaries and cell membranes. NAGASE[15] and YAMAGUCHI[53] in our laboratory demonstrated that fat deficiency — especially EFA-deficiency — induced an increased permeability of capillaries and cell membranes.

(8) Water Balance

As shown in Fig. 1, Fig. 2 and Table 3, primary water balance during the 5 days period before operation showed a larger positive balance in the fat group than in the control group in each experiment. On the other hand, it showed during the 3 days period after operation a smaller balance in the former than in the latter in both experiments.

Table. 3 Water balance for three days after operation.

Group	Days after operation	Water intake	Excretion	Urine specific gravity	Primary water balance	Accumulative water balance
Fat	0	223	374	1027	− 151	− 56
	+ 1	223	358	1020	− 135	
	+ 2	581	351	1026	+ 230	
Control	0	200	229	1034	− 29	+ 122
	+ 1	200	241	1026	− 41	
	+ 2	494	302	1024	+ 192	

Generally speaking, in order to prevent shock due to dehydration during operation and to make the postoperative course smooth, it is necessary to have the patients in a state of slight overhydration prior to operation. Besides, surgical patients are usually somewhat dehydrated preoperatively. From this view-point, too, the rationality of the preoperative fat supply can be well understood.

As is well known, an increased adrenal medullary activity just preoperatively or as anesthesia is induced suppresses renal plasma flow (abbreviated as RPF) and the glomerular filtration rate (abbreviated as GFR). Upon injury, an increased secretion of ACTH and consequently increased adrenal steroid hormone secretion also cause a decreased RPF or retention of sodium. These hormones accelerate antidiuresis following operation. However, the postoperative oliguria in all probability is due to an increased secretion of antidiuretic hormone (abbreviated as ADH) by the posterior pituitary[54)~61)].

There exists in the supraoptic nucleus an osmoreceptor which is responsive to the tonicity of the plasma. The experiments of VERNEY[52] established that the posterior pituitary secretion of ADH is stimulated by an increase in the effective osmotic pressure of extracellular water bathing an osmoreceptor somewhere in the distribution of the internal carotid artery.

LEAF and MAMBY[33] postulated that the "volume receptor" was responsive for the changes in the effective circulating plasma volume. In instances of contracted effective plasma volume, the volume receptor activates the supraoptico-posterior pituitary system, resulting in the secretion of ADH and conservation of water.

The secretion of ADH persists for about 24 hours after surgical invasion, and later the secretion of this hormone ceases. It is well known, however, that anti-diuretic substance in serum is maintained in high concentration for about 3 days after a surgical insult[55)56)]. These findings suggest that inactivation or destruction of ADH secreted by the posterior pituitary is suppressed during this period. It has been postulated that cortisone inactivates or destroys ADH in the liver, and, therefore, the more the hepatic disturbance and adrenal cortical insufficiency are, the more the inactivation or destruction of ADH is delayed[55)54)].

The causes of the urine volume in the fat group during the 3 days after operation being more than in the control group were considered to be that the secretion of ADH via the volume receptor was less in the fat group than in the control group (as mentioned above in the experimental results of circulating plasma volume), and that ADH was inactivated or destroyed more rapidly in the fat group than in the control group. Because, as has been proven by Matsuda[64)] in our laboratory, a supply of fat of good quality is necessary to maintain liver function and the liver glycogen content, and Guggenheim et al. have further pointed out that a shortage of lipotropic substances could cause a remarkable decrease in the liver's ability to destroy ADH which was secreted by the posterior pituitary at the time of a surgical insult. The administration of the fat emulsion maintains the liver glycogen content and the liver function, and supplies sufficiently EFA as lipotropic substances. Therefore, the administration of the emulsion makes inactivation or destruction of ADH in the liver rapid and smooth.

Generally speaking, since postoperative oliguria and retention of water and sodium are so marked during the stage of accelerated secretion of ADH, fluid infusion should be kept to a minimum to avoid edema of the whole body, operative wound and pulmonary complication. Slight dehydration is usually preferable at this stage. From this view-point, too, the rationality and appropriateness of the combined infusion of the fat emulsion with electrolyte solution before and after operation can be well understood.

(9) Water Contents in Various Organs

As shown in Table 5, water contents in the various organs changed markedly from the normal levels in the control group by dehydration or overhydration. On the other hand, these changed more slightly in the fat group as compared to the control group in both experiments. These findings suggested that the administration of the fat emulsion did not bring about changes in water content in the various organs under the influence of dehydration or overhydration, and maintained them

Table. 5 Water content (%) in various organs (mean values).

Group		Liver	Spleen	Kidney	Muscle	Lung	Heart	Adipose tissue
Overhydration	Fat	69.8	78.7	78.1	75.7	76.4	78.6	37.2
	Control	71.2	79.3	79.5	76.1	76.8	80.8	56.7
Dehydration	Fat	69.5	77.6	77.9	75.6	76.1	78.4	36.8
	Control	67.2	77.5	77.3	74.2	75.7	78.0	55.4

at near the normal levels. These data corresponded with the experimental results of TBW.

D. CONCLUSION

The influence of the administration of the fat emulsion on fluid metabolism was investigated experimentally in healthy adult dogs. The following conclusions were reached :

(1) Repeated infusions of the sesame oil emulsion before and after operation maintain body fluid distribution at near the normal level throughout the pre- and postoperative stages. Even in dehydration or overhydration experiments, the administration of the emulsion throughout all the periods does not induce abnormal distribution of body fluid out of the normal level as happened in the control group.

(2) The combined use of the emulsion before operation with RINGER's solution or BES and 5% glucose solution is very effective for the improvement of preoperative dehydration in the body.

Generally speaking, surgical patients tend to be dehydrated before operation and slight preoperative overhydration is preferable to make the postoperative course smooth. Therefore, from these view-points, the combined administration of the sesame oil emulsion with electrolyte solution and isotonic glucose solution is rational.

(3) When the combined use of the fat emulsion with RINGER's solution or BES and 5% glucose solution is continued throughout the pre- and postoperative stages, the postoperative course is very smooth. A significantly abnormal retention of water in the body does not occur in the stage of postoperative oliguria, and the dynamic process of convalescence goes forward smoothly.

(4) The administration of the fat emulsion throughout the pre- and postoperative stages is very effective in the prevention of postoperative shock.

(5) The effects of the fat emulsion on fluid metabolism may be partly explained by the actions which keep the concentration of serum protein and serum albumin normal and are effective on the maintenance of serum colloidal osmotic pressure. However, it should be also taken into consideration that the administration of EFA which are contained abundantly in this sesame oil emulsion suppresses an increased permeability of the capillaries and cell membranes.

Ⅲ. THE INFLUENCE OF POSTOPERATIVE OVERHYDRATION IN EFA-DEFICIENT GASTRECTOMY DOGS

BURR and BURR[35] in 1929, for the first time, listed the EFA-deficient syndrome in rats as follows: (1) marked retardation in growth; (2) development of scaly skin and caudal necrosis; (3) kidney lesions with concomitant hematuria; and (4) death. The specific nutritional significance of fat, especially that of EFA, has been investigated by numerous workers[36,37,38], and it has been demonstrated more clearly that fat has a very important significance as a constant element in the body.

In the previous experiments, healthy adult dogs were used for experimental animals, and, therefore, it cannot be permitted to consider that the experimental

Table. 6 Calories, carbon dioxide elimination and oxygen consumption in oxidation process of various foodstuffs.

Foodstuff	Calories	Water of oxidation	Oxygen	Carbon dioxide
1gm. Carbohydrate	4.1	0.600gm	1.185ml	1.629ml
1gm. Fat	9.3	1.071gm	2.876ml	2.805ml
1gm. Protein	4.1	0.416gm	1.382ml	1.522ml
1gm. Ethylalcohol	7.0	1.170gm		
1gm. Lactic acid	3.6	0.60gm		

1gm of water at body temperature occupies a volume of 1 ml.

results represented immediately those of fluid metabolism in the surgical patients under some pathologic states in clinic. Generally speaking, surgical patients are usually in a state of malnutrition in various degrees because of either the restricted food intake due to dysphagia or cancerous cachexia. JINDO[39], in our laboratory, demonstrated that such patients had a marked decrease of the EFA contents in the body. Accordingly, it is an important problem in surgical metabolism to understand how changes occur in fluid distribution in the body when such patients are subjected to an operation and given excessive water postoperatively. NAGASE[13] and YAMAGUCHI[53] in our laboratory have demonstrated that EFA-deficiency induced structural changes in the cell membranes and an increased capillary permeability, the author investigated again the fact that EFA-deficiency forms the background for the development of acute postoperative pulmonary edema, which had been proven by NAGASE in our laboratory.

A. MATERIALS

(1) EFA-Deficient Dogs

The dogs, which were administered once a day for two months[70] diets composed of such substances as shown in Table 7, were used as the EFA-deficient dogs in this experiment.

Table. 7 The following diet was administered for two months in the fat-deficient group.

	weight (g/10kg)	Cal.	Protein (g)	Fat (g)	Carbohydrate (g)	Nacl (g)
Rice	130	448	7.7	2.61	98.6	0
Fish (Salted, dried)	40	98.5	21.4	1.32	0	2.2
Hen's egg (white)	5	2.5	0.51	0	0	0
Nacl	1.0	0	0	0	0	1.0
Water	450	0	0	0	0	0
Total	626	549.0	29.61	3.93	98.6	3.2

Such EFA-deficient dogs were divided into two groups: The first group was infused intravenously with 5% glucose solution or isotonic saline solution or RINGER'S solution or subcutaneously with 5% glucose solution during the 5 days before operation and a few days after operation (the EFA-deficient group). The second group was infused intravenously with 2cc per kg of body weight of the sesame oil emulsion diluted by each solution during the same periods. When, however, 5% glucose solution was infused subcutaneously, the fat emulsion was not diluted by it and infused singly intravenously very slowly by syringe without side effects (the fat group).

After operation, as shown in Table 8, the administration of excessive water (60～120cc per kg of body weight) was carried out by infusion.

Various vitamins were administered on both groups as in the previous experiments.

The same anesthesia and the same operation were performed as in the previous experiments.

B. METHODS

(1) Body weight, (2) TBW, (3) ECW, (4) ICW, (5) circulating plasma volume, (6) circulating blood volume, (7) Ht., (8) concentration of the serum protein, (9) circulating serum protein, (10) serum colloidal osmotic pressure, (11) water balance and (12) water contents in various organs etc. were measured or calculated by the same methods or procedures as in the previous experiments.

(13) Mean Corpuscular Hemoglobin (M. C. H.)[38]

$$\text{M. C. H. } (\gamma\gamma) = \frac{\text{Hb (g/dl)}}{\text{R} (10^6/\text{mm}^3)} \times 10$$

Mean Corpuscular Volume (M. C. V.)

$$\text{M. C. V. } (\mu^3) = \frac{\text{Ht. } (\%)}{\text{R} (10^6/\text{mm}^3)} \times 10$$

Mean Corpuscular Hemoglobin Concentration

$$\text{M. C. H. C. or M. C. C. } (\%) = \frac{\text{Hb (g/dl)}}{\text{Ht. } (\%)} \times 10$$

Blood samples were taken from the femoral vein.

An anti-coagulant was used. The measurements of Hb, erythrocyte count (R) and Ht. were done as fast as possible.

(14) Na- and K-Concentration in the Serum and Ascites

They were measured by flame photometer[24] in co-operation with TANAKA[71] in our laboratory.

(15) Serum Icterus Index[38]

This was represented by MEULENGRACHT's icterus index.

(16) Histological Examination of the Lung

The bilateral carotid arteries were cut across allowing the blood to flow freely. After the blood flow ceased, a part of the lung was dissected and fixed with 10% formalin solution and examined histologically with hematoxylin-eosin staining.

C. RESULTS

(1) Infusions of excessive water after operation were performed by various kinds of solutions, various volumes of solutions and various methods of infusions as shown in Table 8.

In the fat group, acute postoperative pulmonary edema[72)~80] did not occur at all, and all the cases survived in these experiments. On the other hand, in the EFA-

Table. 8 Effects of postoperative overhydration.

Group	Volume of administered solution (cc/kg)	Method of infusion		Fat group Result Survived or died	Fat group Result A.P.P.E.	Fat-deficient group Result Survived or died	Fat-deficient group Result A.P.P.E.
5 % Glucose solution	120	Sub-cutaneously		survived	–	died at 3°15' after infusion on the 2nd postoperative day	+
	80	Sub-cutaneously		survived	–	survived	–
	100	Sub-cutaneously		survived	–	died at 1°30' after infusion on the 2nd postoperative day	–
	100	Intra-venously	Hyaluronidase 100U/kg	survived	–	died at 5° after infusion on the 1st postoperative day	–
	100	Intra-venously		survived	–	died at 2°5' after infusion on the 2nd postoperative day	+
	80	Intra-venously		survived	–	survived	–
Isotonic saline solution	100	Intra-venously		survived	–	died at 3°20' after infusion on the 2nd postoperative day	+
	80	Intra-venously		survived	–	survived	–
RINGER's solution	100	Intra-venously		survived	–	died at 2°30' after infusion on the 2nd postoperative day	+
	80	Intra-venously		survived	–	survived	–

A.P.P.E. = Acute postoperative pulmonary edema

deficient group, 6 dogs out of 10 died, and 4 dogs out of them showed histologically the typical figures of acute postoperative pulmonary edema which were accompanied with a marked intraalveolar accumulation of fluid. Death occurred on the 1st or the 2nd day after operation. It was made clear, therefore, that the EFA-deficient dogs were subjected easily to typical acute postoperative pulmonary edema following postoperative overhydration and died on the 1st or the 2nd day after operation when excessive water of more than 100cc per kg of body weight was infused after operation independently of any kinds of solutions or methods of infusions (Photo).

(2) Body Weight (Fig. 7, Fig. 9 and Fig. 11)

The maintenance of the body weight before operation in the fat group was better than in the EFA-deficient group. In the EFA-deficient group, the body weight increased markedly following the postoperative overhydration. On the other hand, in the fat group such a remarkable increase of it could not be seen.

(3) TBW

As shown in Fig. 8, Fig. 10 and Fig. 12, TBW increased slightly before operation in both groups, but after operation in the EFA-deficient group TBW increased remarkably following the administration of excessive water after operation. On the

Fig. 7 Changes in urine volume, urine specific gravity, water balance and body weight in dogs which were infused intravenously with 5 % glucose solution.

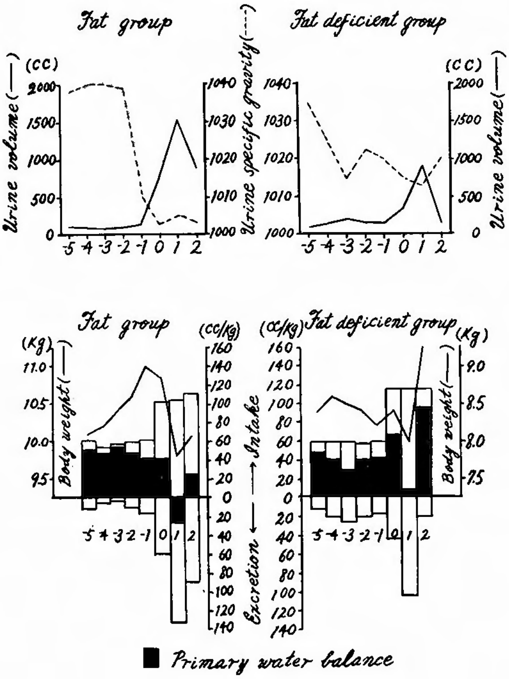


Fig. 8 Changes in fluid distribution in dogs which were infused intravenously with 5 % glucose solution.

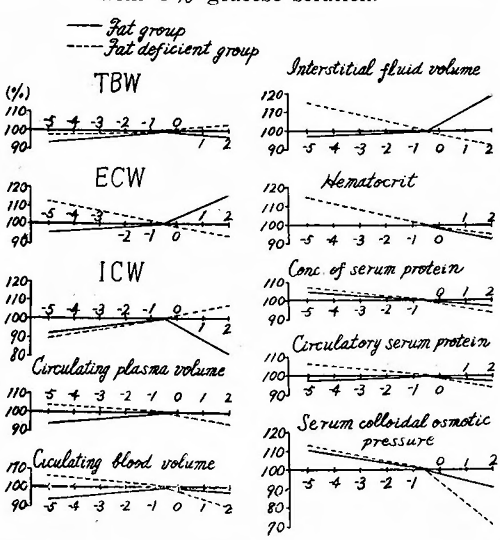


Fig. 9 Changes in urine volume, urine specific gravity, water balance and body weight in dogs which were infused intravenously with isotonic saline solution.

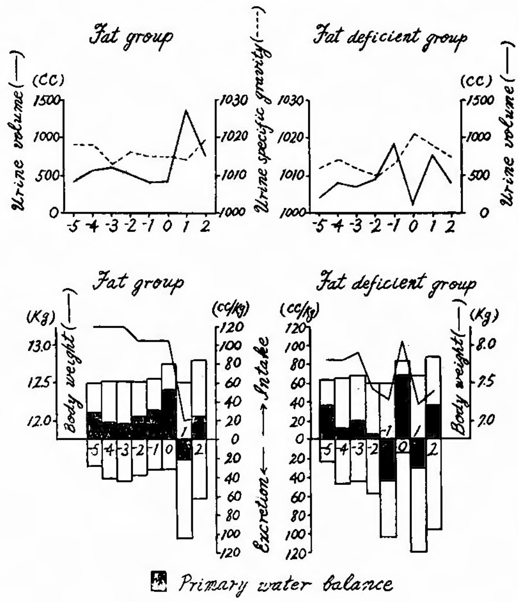


Fig. 10 Changes in fluid distribution in dogs which were infused intravenously with isotonic saline solution.

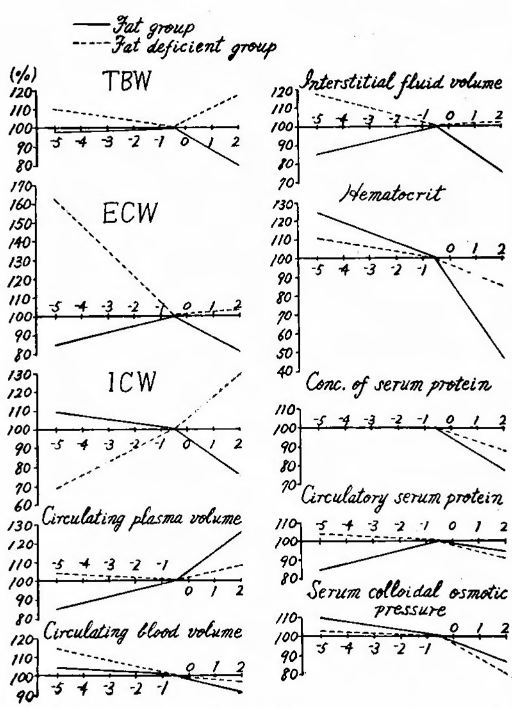


Fig. 11 Changes in urine volume, urine specific gravity, water balance and body weight in dogs which were infused intravenously with Ringer's solution.

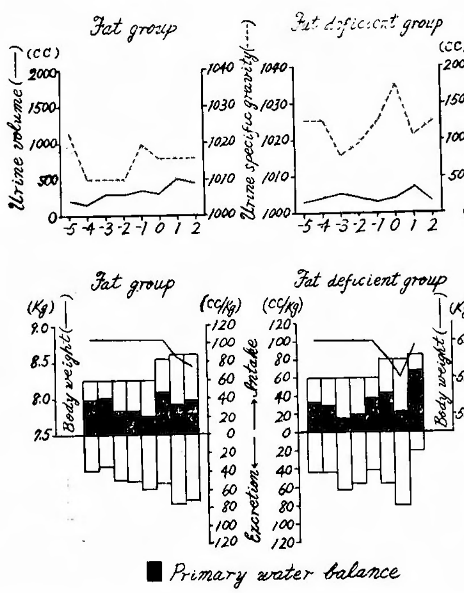
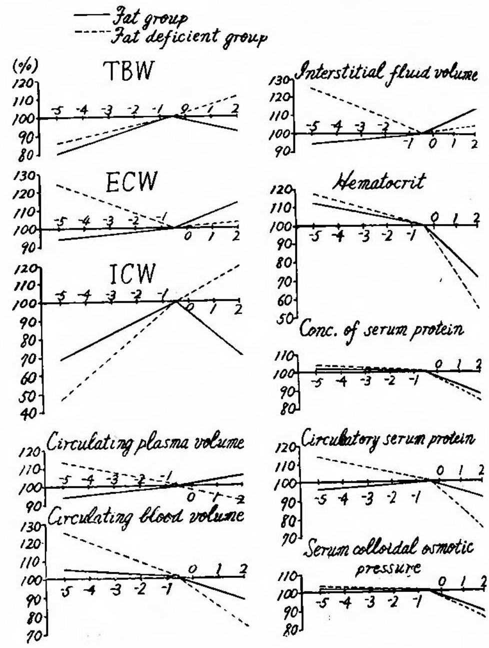


Fig. 12 Changes in fluid distribution in dogs which were infused intravenously with Ringer's solution.



other hand, in the fat group it had rather a tendency to decrease in spite of the administration of excessive water after operation.

(4) ECW and ICW (Fig. 8, Fig. 10 and Fig. 12)

Before operation in the fat group they expanded slightly in parallel with each other and a state of preoperative dehydration was ameliorated. On the other hand, in the EFA-deficient group during this period, the body water showed such an unbalanced distribution that the ICW expanded in spite of a reduction in ECW before operation.

In addition to these states, when the dogs were subjected to operation and loaded postoperatively with infusions of excessive water, ICW expanded more markedly in the EFA-deficient group. On the other hand, in the fat group the development of the expansion of ICW was suppressed at the sacrifice of the expansion of ECW.

(5) Circulating Plasma Volume, Circulating Blood Volume, Ht., Concentration in Serum Protein and Serum Colloidal Osmotic Pressure

Circulating plasma volume and circulating blood volume in the fat group were less changeable and were maintained at nearer the normal level throughout the pre- and postoperative stages than in the EFA-deficient group. Moreover, the EFA-deficient dogs were inclined to show hemoconcentration after operation (Fig. 8, Fig. 10 and Fig. 12).

(6) Water Balance

As shown in Fig. 7, Fig. 9, Fig. 11, Table 9, Table 10, Table 11, Table 12 and Table 13, independently of the kinds and methods of infusion, primary water balance during the 5 days before operation was more positive in the fat group than in the EFA-deficient group, but during the 3 days after operation it was larger in the EFA-deficient group than in the fat group.

Table. 9 Water balance in dogs infused subcutaneously with 5 % glucose solution.

Fat group

Days of exam.	Intake		Excretion		Primary water balance		Accumulative balance	
	cc	cc/kg	cc	cc/kg	cc	cc/kg	cc	cc/kg
− 5	631	63.1	110	11.0	521	52.1		
− 4	548	54.3	70	7.0	478	47.3		
− 3	631	61.8	70	6.8	561	55.0	2537	246.2
− 2	631	60.0	105	10.0	526	50.0		
− 1	631	58.4	180	16.6	451	41.8		
0	1140	103.0	680	61.4	460	41.6		
+ 1	1140	104.5	1450	132.9	−310	−28.4	390	39.4
+ 2	1140	115.8	900	89.6	240	26.2		

Fat-deficient group

Days of exam.	Intake		Excretion		Primary water balance		Accumulative balance	
	cc	cc/kg	cc	cc/kg	cc	cc/kg	cc	cc/kg
− 5	510	60.3	110	12.9	400	47.4		
− 4	510	60.3	175	20.6	335	39.7		
− 3	510	58.0	235	26.4	275	31.6	1725	202.8
− 2	510	59.7	145	17.0	365	42.7		
− 1	510	60.3	160	18.9	350	41.4		
0	935	114.0	370	45.0	565	69.0		
+ 1	935	111.0	900	106.8	35	1.2	1375	169.2
+ 2	935	115.0	160	19.0	775	96.0		

Table. 10 Water balance in dogs infused subcutaneously with 5 % glucose solution and Hyaluronidase.

Fat group

Days of exam.	Intake		Excretion		Primary water balance		Accumulative balance	
	cc	cc/kg	cc	cc/kg	cc	cc/kg	cc	cc/kg
− 5	630	61.8	220	21.7	410	40.1		
− 4	630	60.1	350	33.4	280	26.7		
− 3	630	59.5	360	34.1	270	25.4	1440	137.3
− 2	630	58.9	430	40.2	200	18.7		
− 1	630	59.5	350	33.1	280	26.4		
0	1020	97.2	800	76.2	220	21.0		
+ 1	1020	102.0	1000	100.0	20	2.0	260	25.0
+ 2	1020	103.0	1000	101.0	20	2.0		

Fat-deficient group

Days of exam.	Intake		Excretion		Primary water balance		Accumulative balance	
	cc	cc/kg	cc	cc/kg	cc	cc/kg	cc	cc/kg
−5	510	59.3	210	24.4	300	34.9		
−4	510	58.6	310	35.6	200	23.0		
−3	510	58.0	210	23.9	300	34.1	1220	138.9
−2	510	56.8	340	37.9	170	18.9		
−1	510	57.0	260	29.0	250	28.0		
0	900	102.1	720	81.6	180	20.5		
+1	900	103.2	680	77.9	220	25.3	1050	122.7
+2	900	106.5	250	29.6	650	76.9		

Table. 11 Water balance in dogs infused intravenously with 5% glucose solution.

Fat group

Days of exam.	Intake		Excretion		Primary water balance		Accumulative balance	
	cc	cc/kg	cc	cc/kg	cc	cc/kg	cc	cc/kg
−5	664	59.8	440	39.6	224	20.2		
−4	664	60.3	250	22.7	414	37.6		
−3	664	59.3	320	28.6	344	30.7	1640	146.2
−2	664	58.2	340	29.8	324	28.4		
−1	664	58.2	330	28.9	334	29.3		
0	880	76.5	550	47.8	330	28.7		
+1	880	80.0	900	82.6	−20	−1.8	640	58.6
+2	880	81.6	550	52.9	330	31.7		

Fat-deficient group

Days of exam.	Intake		Excretion		Primary water balance		Accumulative balance	
	cc	cc/kg	cc	cc/kg	cc	cc/kg	cc	cc/kg
−5	710	69.5	480	48.6	230	20.9		
−4	710	69.5	360	37.7	350	31.8		
−3	710	69.5	240	27.2	470	42.3	1490	134.1
−2	710	69.5	420	43.6	290	25.9		
−1	710	69.5	560	56.3	150	13.2		
0	910	79.8	630	54.2	280	24.6		
+1	910	79.1	980	85.8	−70	−6.7	670	62.5
+2	910	80.5	450	32.9	460	44.6		

Table. 12 Water balance in dogs infused intravenously with isotonic saline solution.

Fat group

Days of exam.	Intake		Excretion		Primary water balance		Accumulative balance	
	cc	cc/kg	cc	cc/kg	cc	cc/kg	cc	cc/kg
− 5	796	59.8	400	30.0	396	29.8		
− 4	796	61.2	550	42.3	246	18.9		
− 3	796	61.2	590	45.3	206	15.9	1540	118.3
− 2	796	61.2	500	38.4	296	22.8		
− 1	796	62.2	400	31.3	396	30.9		
0	1040	81.3	400	31.3	640	50.0		
+ 1	780	61.0	1320	103.2	− 540	− 42.2	390	32.0
+ 2	1040	86.7	750	62.5	290	24.2		

Fat-deficient group

Days of exam.	Intake		Excretion		Primary water balance		Accumulative balance	
	cc	cc/kg	cc	cc/kg	cc	cc/kg	cc	cc/kg
− 5	492	63.1	200	25.6	292	37.5		
− 4	492	63.1	400	51.3	92	11.8		
− 3	492	67.4	340	46.6	152	20.8	200	29.0
− 2	492	61.5	460	57.5	32	4.0		
− 1	492	60.7	860	106.1	− 368	− 45.4		
0	656	82.1	100	12.6	556	69.5		
+ 1	492	68.4	760	121.9	− 268	− 33.5	554	73.0
+ 2	656	91.2	390	54.2	266	37.0		

Table. 13 Water balance in dogs infused intravenously with Ringer's solution.

Fat group

Days of exam.	Intake		Excretion		Primary water balance		Accumulative balance	
	cc	cc/kg	cc	cc/kg	cc	cc/kg	cc	cc/kg
− 5	540	61.4	200	22.7	340	38.7		
− 4	540	61.4	160	18.5	380	42.9		
− 3	540	61.4	310	35.2	230	26.2	1370	155.6
− 2	540	61.4	300	34.1	240	27.3		
− 1	540	61.4	360	40.9	180	20.5		
0	720	81.9	300	31.1	400	47.8		
+ 1	720	85.8	470	56.0	250	29.8	950	113.8
+ 2	720	86.8	420	50.6	300	36.2		

Fat-deficient group

Days of exam.	Intake		Excretion		Primary water balance		Accumulative balance	
	cc	cc/kg	cc	cc/kg	cc	cc/kg	cc	cc/kg
−5	360	60.0	150	25.0	210	35.0		
−4	360	60.0	170	28.3	190	31.7		
−3	360	60.0	270	45.0	90	15.0	840	140.1
−2	360	60.0	230	38.3	130	21.7		
−1	360	60.0	140	23.3	220	36.7		
0	480	80.0	220	36.7	260	43.3		
+1	480	81.4	360	59.6	120	21.8	740	130.0
+2	480	86.5	120	21.6	360	64.9		

(7) Water Contents in Various Organs

As shown in Table 14, they were markedly larger in the EFA-deficient group than in the fat group. These organs could be enumerated from the largest one to the smallest one in water content as follows:

In the fat group,

lung > a part of anastomosis > heart > intestine > spleen > cerebrum > muscle > liver > pancreas

In the EFA-deficient group,

lung > a part of anastomosis > intestine > heart > spleen = cerebrum > liver > muscle > pancreas

And especially, water contents in the lung and a part of anastomosis increased more markedly in the EFA-deficient group than in the fat group.

Table. 14 Water content (%) in various organs.

Group	No.	Lung	Heart	Liver	Spleen	Intestine	Muscle	Cerebrum	Pancreas	Part of anastomosis
Fat	1	80.3	76.9	73.0	77.0	76.7	72.8	75.0	56.5	78.8
	2	80.0	78.3	73.7	77.1	79.8	73.4	75.8	76.2	78.7
	3	79.6	77.4	70.9	78.3	77.1	77.1	78.7	73.4	78.9
	4	78.2	77.9	73.1	77.1	76.9	74.2	76.4	71.3	77.4
	5	79.8	78.6	72.6	78.2	78.2	74.7	75.1	70.1	79.0
	6	78.5	77.7	71.5	77.0	77.6	73.3	75.0	68.7	77.9
	Mean	79.4	77.8	72.5	77.5	77.7	74.3	76.0	69.4	78.5
Fat-deficient	1	84.2	79.5	77.0	77.4	80.8	80.0	79.8	74.8	82.8
	2	83.5	80.7	81.2	79.3	81.8	77.2	78.2	80.5	82.5
	3	83.2	81.8	71.9	81.1	80.7	80.7	80.9	80.3	82.6
	4	82.1	81.6	75.0	78.6	78.9	76.8	78.3	78.0	79.8
	5	82.8	79.9	78.1	79.7	79.6	77.4	78.1	78.7	81.0
	6	81.8	80.2	75.0	79.3	79.4	78.1	79.8	77.6	79.3
	Mean	82.9	80.1	78.5	79.2	80.2	78.4	79.2	78.3	81.3

(8) M. C. H., M. C. V. and M. C. H. C.

M. C. H. was usually larger in the EFA-deficient group than in the fat group.

M. C. V. increased abruptly on the 2nd day after operation in the EFA-deficient group (Fig. 13 and Fig. 14).

Fig. 13 Changes in M.C.H., M.C.V. and M.C.C. in dogs which were infused intravenously with 5 % glucose solution.

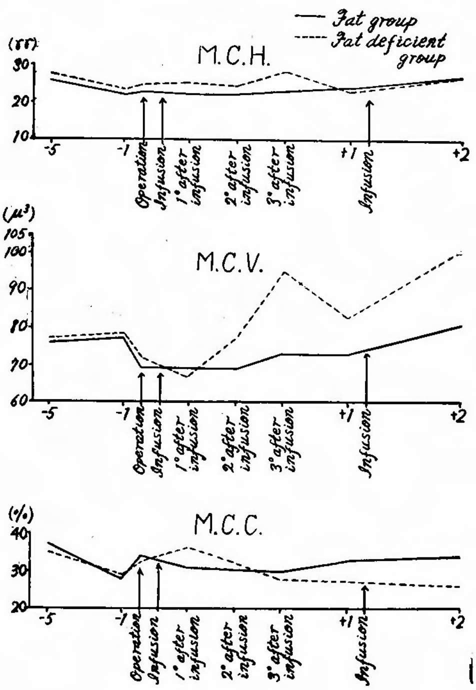
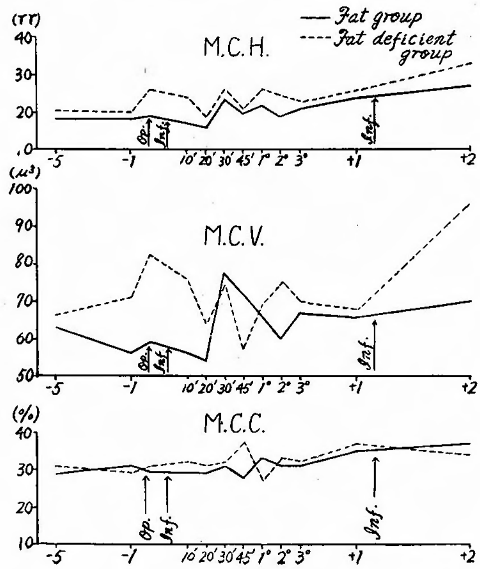


Fig. 14 Changes in M.C.H., M.C.V. and M.C.C. in dogs which were infused intravenously with isotonic saline solution.



(9) Peritoneal Permeability

When an isotonic glucose solution is infused into the peritoneal cavity[31] of the experimental animals, the changes in concentration of the electrolytes and water volume initiate a mechanism to re-establish osmotic equilibrium between the extra-cellular fluid and the infused solution in the peritoneal cavity. The extracellular fluid will become hypotonic and water will move from the extracellular to the intracellular compartment to maintain total body water tonicity, and circulatory failure will be induced as a result of the decline in circulating plasma volume.

Also, in this experiment, 50cc per kg of body weight of 5% glucose solution were infused respectively into the peritoneal cavity of the experimental dogs, which were divided into two groups : the first group was a healthy adult dog, the second was an EFA-deficient dog. At 1, 2, 3, 4 and 5 hours after infusion into the peritoneal cavity, each 5cc of ascites was drawn and each electrolyte concentration (Na^+ and K^+) in the ascites was measured with the flame photometer. At the same time, blood samples were taken from the femoral vein, and each electrolyte concentration in the serum was measured by the same method. Changes of them were then compared with each other.

Table. 15 Changs in concentration of electrolytes (Na, K) in serum and ascites after infusing into the peritoneal cavity with 5 % glucose solution.

Fat group

Time after infusion	Serum Na (mEq/L)	Serum K (mEq/L)	Ascites Na (mEq/L)	Ascites K (mEq/L)
0°	131.2	3.28	0	0
1°	131.0	3.40	67.4	1.03
2°	129.3	3.45	81.6	1.96
3°	129.2	3.48	92.2	2.47
4°	129.2	3.42	98.6	2.54
5°	128.5	3.47	107.3	3.15

(Survived
No changes in Peritoneum)

Fat-deficient group

Time after infusion	Serum Na (mEq/L)	Serum K (mEq/L)	Ascites Na (mEq/L)	Ascites K (mEq/L)
0°	130.5	3.28	0	0
1°	130.2	3.44	71.8	1.62
2°	127.8	3.52	90.7	2.43
3°	127.6	3.59	108.2	2.73
4°	127.1	3.44	111.5	2.97
5°	126.5	3.52	118.3	3.36

(died at 7° after infusion
Large subperitoneal hematomas were found.)

It was demonstrated that the electrolyte concentration in the ascites increased more rapidly and Na^+-concentration in the serum decreased more rapidly in the EFA-deficient dog than in the healthy adult dog (Table 15).

These findings suggested that the EFA-deficient dog had an increased peritoneal permeability to water and electrolytes, and were subjected easily to water intoxication. The EFA-deficient dog died suddenly at about 7 hours after infusion into the peritoneal cavity of the 5% glucose solution. It was dissected immediately, and it was found that multiple large hematomas in the peritoneum were formed. It was evident from this observation that EFA was concerned with the capillary resistance. The cause of death could be considered to be circulatory failure and water intoxication [82)83)].

(10) MEULENGRACHT's Icterus Index

MEULENGRACHT's icterus indices in the serum were measured in the dogs which were infused subcutaneously with 100cc per kg of body weight of a 5% glucose

Table. 16

Change in MEULENGRACHT's icterus index in fat-deficient dog infused subcutaneously postoperatively once a day with 5 % glucose solution 100 cc/kg and hyaluronidase 100 U./kg.

Days of examination	− 5	− 1	0	+ 1	+ 2
MEULENGRACHT	1	1	1	7	8

Change in MEULENGRACHT's icterus index in fat-sufficient dog infused subcutaneously postoperatively once a day with 5 % glucose solution 100 cc/kg and hyaluronidase 100 U./kg.

Days of examination	5	− 1	0	+ 1	+ 2
MEULENGRACHT	1	1	1	2	2

solution plus 100 U. per kg of body weight of hyaluronidase after operation. As shown in Table 16, it was recognized that the icterus indices increased abnormally in the EFA-deficient dog after operation. At the same time, in this icteric dog, the direct reaction was negative and the indirect reaction was positive by the method of HIJMANS VAN DEN BERGH. Therefore, it was considered that the abnormal increase in the icterus indices was based on hemolysis following the postoperative infusion with 5% glucose solution plus hyaluronidase. On the other hand, in the fat dog which was infused with the same solutions, such abnormal increase in the icterus indices was not recognized.

D. DISCUSSION

The influence of the postoperative infusion of excessive water on the fluid metabolism in the EFA-deficient gastrectomy dogs was investigated in this section. As the results of this study, it could be found that the following findings were common independently of the kinds or methods of the infusions.

(1) The EFA-deficient animal had an usual tendency for preoperative dehydration.

When the fat emulsion was given simultaneously with the various vitamins and solutions, such as RINGER's solution or isotonic saline solution or 5% glucose solution etc., the state of preoperative dehydration was ameliorated and both the extracellular and intracellular water volume expanded slightly in parallel with each other. Therefore, the state of preoperative slight overhydration which is preferable in order to make the postoperative course smooth, could be brought about with ease by the administration of fat emulsion.

On the other hand, when the electrolyte solution or isotonic glucose solution was given only without the simultaneous use of the fat emulsion in the EFA-deficient animals during preoperative stage, body water had such an unbalanced distribution that the intracellular compartment expanded in spite of reduction in the extracellular water volume, which was not preferable to operation.

(2) In addition to this state, when the electrolyte solution or isotonic glucose solution was administered in excess without the simultaneous use of the fat emulsion after operation in the EFA-deficient animals, the administered water in excess during the period of antidiuresis was not associated with an increase in the urine flow rate. It was retained in the body and the intracellular compartment expanded abnormally. These were the most characteristic findings in the EFA-deficient animals.

On the other hand, even though excessive water was administered after operation, when the fat emulsion was given simultaneously with electrolyte solution or isotonic glucose solution throughout the pre- and postoperative stages even in such EFA-deficient animals, the antidiuresis following the surgical insult was slighter and the retention of water in the body was less, moreover the extracellular compartment expanded without the abnormal expansion of intracellular compartment which means water intoxication.

The reasons why EFA-deficiency induced the remarkable cellular overhydration with the postoperative administration of excessive water, and why, on the other hand, if the administration of the fat emulsion which contained abundantly the essential fatty acids was continued throughout the pre- and postoperative stages, retention of water was slighter and the retained water was caught by the extracellular compartment and did not move rapidly from the extracellular to the intracellular compartment by the postoperative overhydration, were considered as follows:

Though it is necessary, of course, to consider the problems of serum colloidal osmotic pressure or the secretion of ADH by the posterior pituitary following surgical insult or the liver's ability to destroy ADH as mentioned in the previous section, we should also consider NAGASE's and TAMAKI's[84] experimental results showing that the ability of the adrenal cortices to produce or secrete glucocorticoids is impaired by EFA-deficiency, and that the adrenals of the EFA-deficient animals cannot respond sufficiently to the increased demand for glucocorticoids in the body subjected to such stresses as infection, operative insult and trauma — this phenomenon they speak of as "decrease of adrenocortical capacity". Currently, it has been reported by KRAMÁR et al.[85)86] that the stress usually induced a rise of the permeability of the capillary walls and cell membranes. In normal animals, however, the glucocorticoids which are secreted satisfactorily by the adrenal cortices[87)~90] under various stresses suppress an abnormal rise of permeability of capillaries and cell membranes. Therefore, such reaction of adrenal cortices against stimuli or stresses of all varieties is rational under various stresses.

When excessive water is administered to the EFA-deficient animals during such period that the EFA-deficiency induces an abnormal rise of permeability of capillaries and cell membranes following the stress, it moves rapidly from the capillaries to the extracellular compartment and from the extracellular to the intracellular compartment, and therefore socalled "water intoxication", mild and severe, is caused by cellular overhydration.

In addition, it seems most likely that acute postoperative pulmonary edema was induced as a partial phenomenon of water intoxication in these cases. As shown in the experimental results of water contents in various organs, it seems that retained water tended to move more rapidly from the capillaries to the intracellular compartment in the lung and the operative wound than in the other organs in the EFA-deficient animals. Acute postoperative pulmonary edema has serious influence on the body and the clinical manifestations of acute postoperative pulmonary edema are dramatic, because the lung plays an important role in the fulfilment of respiratory function. As shown in this experiment, when the manifestations of acute postoperative pulmonary edema are recognized, it should be considered that the intracellular compartment also expands significantly at the same time.

Now, we should consider that an abnormally increased permeability of the capillaries and cell membranes occurred not only under conditions of stress in the EFA-deficient animals, but also it existed under usual conditions, from the experimental results of the preoperative fluid distribution in the EFA-deficient animals. Therefore, it is rational to believe that the EFA play an important role in maintaining the normal permeability of capillaries and cell membranes as one of their structural components[91] under usual conditions.

On the whole, the causes of the high incidence of water intoxication after operation in the EFA-deficient dogs could be summerized as follows:

EFA-deficiency, on the one hand, induces a deficiency of the lipoprotein constituents of tissue cells and provokes structural changes of the capillary walls and cell membranes and increases permeability of them, and, on the other hand, so-called "decrease of adrenocortical capacity" due to EFA-deficiency renders it impossible to suppress the remarkably increased permeability of capillaries and cell membranes under various stresses. Moreover, the liver's ability to destroy ADH, which is secreted by the posterior pituitary after operation, decreases much more in the EFA-deficient dogs as a result of the shortage of EFA which play also an important role as lipotropic substances and are necessary to maintain liver function and liver glycogen content. These changes all together form a background for the development of postoperative water intoxication. In addition to these states, when excessive water is administered, abnormal water retention occurs and the retained water moves rapidly to the intracellular compartment and water intoxication develops.

Urine volume during the 3 days after operation was usually less in the EFA-deficient dogs than in the fat treated dogs. This finding suggested that destruction or inactivation of ADH in the liver lowered as the result of disturbances in the liver function as mentioned above.

Sinclair[91] pointed out that EFA-deficiency induced an increased fragility of the erythrocytes. In our experiment, when 100cc per kg of body weight of 5% glucose solution was infused subcutaneously repeatedly with 100 U. per kg of body weight of hyaluronidase after operation in the EFA-deficient dogs, icterus occurred which was considered to be due to hemolysis. These results seemed to agree with those obtained by Sinclair. Moreover, these results seemed to suggest that EFA-deficiency induced a "decrease of adrenocortical capacity." Also Opsahl[92] and Winter[93] et al. have demonstrated that ACTH and cortisone decreased activity of hyaluronidase in spreading factor experiments using India ink and dyes. And in addition, patients with Cushing's syndrome show less hyaluronidase activity than normals, and patients with Addison's disease are apt to show an increase in hyaluronidase activity which is decreased with cortisone therapy.

Experimental results of M. C. V. showed that EFA played an important role in maintaining the normal permeability of the membranes of erythrocytes.

E. CONCLUSION

The influence of postoperative overhydration on the fluid metabolism in the EFA-deficient dogs was experimentally studied and the following conclusions were obtained:

(1) When the EFA-deficient animal undergoes a surgical insult, the improvement of the nutritional state of the animal with EFA-deficiency is a very important treatment from the view-point of the fluid metabolism in the body.

(2) When the EFA-deficient animal is subjected to an operation without improvement of the EFA-deficiency in the body and is administered excessive water after operation, the administered water is abnormally retained in the body and the retained water moves rapidly into the intracellular compartment and water intoxication or acute postoperative pulmonary edema is frequently induced.

(3) When the animal undergoes a surgical insult and postoperative overhydration after the nutritional state of the animal with EFA-deficiency was improved by supplying sufficient EFA which are contained abundantly in the sesame oil emulsion, abnormal retention of water after operation is less than in the EFA-deficient animal, and the extracellular space expands only without the development to the expansion of the intracellular space, and water intoxication or acute postoperative pulmonary edema is not caused by the postoperative administration of excessive water.

Therefore, in order to gain success in operation, the nutritional state of the patients with malnutrition due to restricted food intake or cancerous cachexia should be improved by every possible means throughout the pre- and postoperative stages. As one of the available means, administration of the fat emulsion containing abundant EFA results not only in a remarkable improvement of the nutritional state of the patients but also in preventing the development of water intoxication or acute postoperative pulmonary edema.

(4) The reasons why the EFA-deficiency easily induces water intoxication or acute postoperative pulmonary edema following postoperative overhydration are considered as follows:

There is an abnormally increased permeability of the capillaries and cell membranes even under usual conditions in the EFA-deficient animal.

When such an animal is subjected to an operation, the permeability of the capillaries and cell membranes increases more and more. This is because the secretion of glucocorticoids by the adrenal cortices is impaired by EFA-deficiency under such stress and the adrenals of the EFA-deficient animal cannot respond satisfactorily to the increased demand for glucocorticoids which suppress the increased permeability of capillaries and cell membranes.

In addition, EFA play an important role as lipotropic substances and are important in maintaining liver function and liver glycogen content. So, EFA-deficiency causes a marked decrease in the liver's ability to destroy or inactivate ADH which is secreted by the posterior pituitary following surgical invasion, and, therefore, EFA-deficiency induces marked postoperative oliguria and an abnormal retention of water after operation.

Tht author wishes to express his sincere gratitude to Dr. Y. Hikasa, the lecturer of our division, for his helpful suggestions and kind guidance in the course of the work.

〔 Photo 〕

Photo 1 (Fat group)

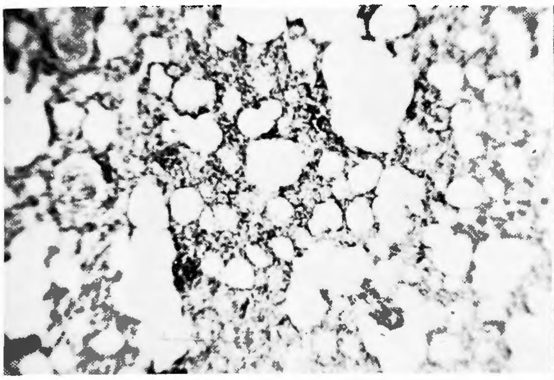


Photo 1′ (Fat-deficient group)

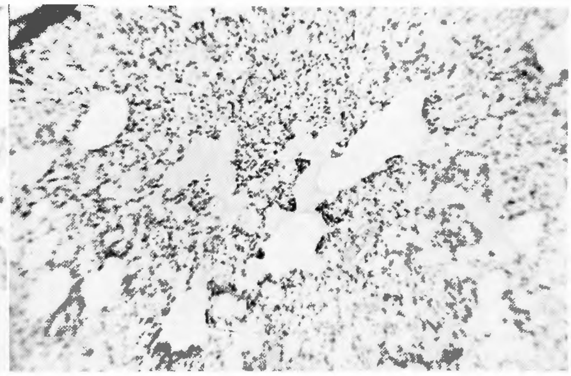


Photo 1 and Photo 1′: 120cc per kg of body weight of 5 % glucose solution were administered subcutaneously postoperatively once a day.

Photo 2 (Fat group)

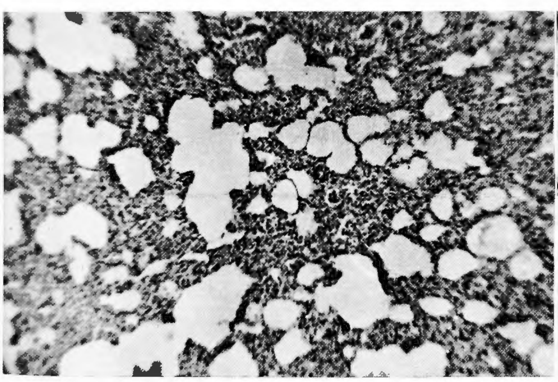


Photo 2′ (Fat-deficient group)

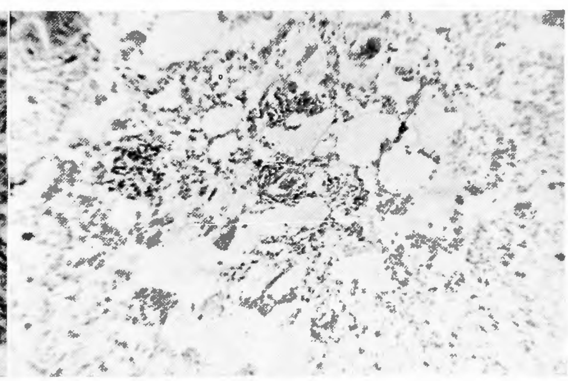


Photo 2 and Photo 2′: 100cc per kg of body weight of 5 % glucose solution were administered intravenously postoperatively once a day.

Photo 3 (Fat group)

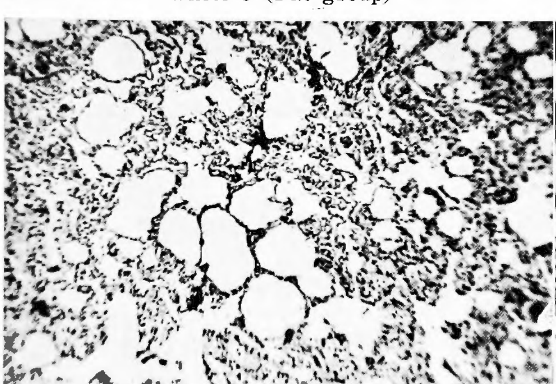


Photo 3′ (Fat-deficient group)

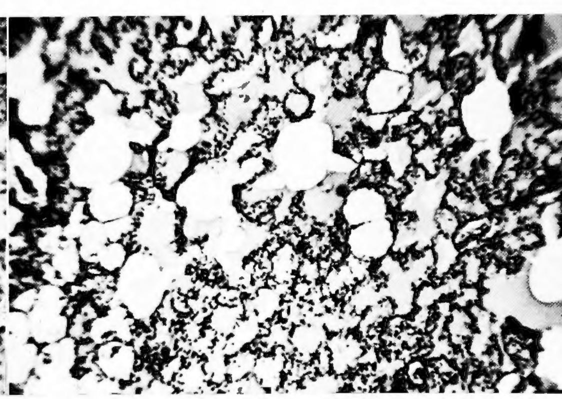


Photo 3 and Photo 3′: 100cc per kg of body weight of isotonic saline solution were administered intravenously postoperatively once a day.

Photo 4 (Fat group) Photo 4′ (Fat-deficient group)

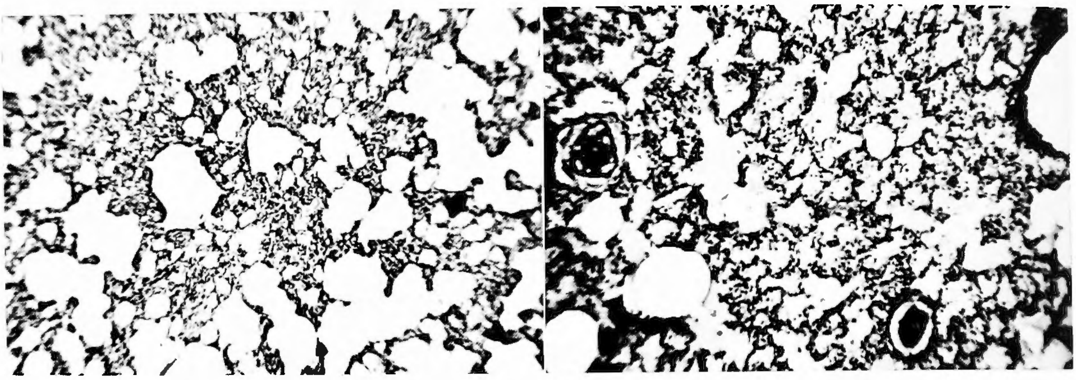


Photo 4 and Photo 4′: 100cc per kg of body weight of RINGER's solution were administered intravenously postoperatively once a day.

REFERENCES

1) Bernard, Claude: Leçon sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme. Paris, Baillère, 1859.
2) Canon, W. B.: The wisdom of the body. New York, Norton, 1932.
3) Moore, F. D.: Bodily changes in surgical convalescence. Ann. Surg., **137**, 289, 1953.
4) Moore, F. D. and Ball, M. R.: The metabolic response to surgery. Springfield, Ill, Charles C Thomas, 1953.
5) Hikasa, Y. et al.: The ground work and practice in the supply of fats (1). Shinryo, **11**, 922, 1958.
6) Hikasa, Y. et al.. The ground work and practice in the supply of fats (2). Shinryo, **11**, 1041, 1958.
7) Hikasa, Y. et al.: Parenteral administration of fats. (1) Fat metabolism in vivo, studied with fat emulsion. Arch. Jap. Chir., **27**, 396, 1958.
8) Hikasa, Y. et al.: Parenteral administration of fats. (2) Clinical application of fat emulsion. Arch. Jap. Chir., **27**, 736, 1958.
9) Hikasa, Y. et al.: Parenteral administration of fats. (3) Qualitical investigation on nutritional effects of fats and recent studies on fat metabolism in vivo. Arch. Jap. Chir., **28**, 835, 1959.
10) Hikasa, Y. et al.: Nutritional significances of fats. Clinic All Round, **1**, 116, 1958.
11) Hikasa, Y. et al.: On the studies of fat metabolism and its nutritional significance following administration of fat emulsion. Saishin-igaku, **13**, 2278, 1958, **13**, 2586, 1958, **13**, 2954, 1958.

12) Hikasa, Y. et al.: Nutritional problems on fats. Geka-shinryo, **1**, 332, 1959, **2**, 117, 1960, **2**, 253, 1960, **2**, 386, 1960, **2**, 648, 1960, **2**, 931, 1960.
13) Hikasa, Y. et al.: Pathogenesis of acute postoperative pulmonary edema. Sogo-rinsho, **9**, 1750, 1960.
14) Kuyama, T.: Clinical studies on the nutritional effects of intravenous administration of fat emulsion. Arch. Jap. Chir., **27**, 64, 1958.
15) Hanafusa, S.: Clinical studies on the nutritional effects of fat emulsion administered intravenously and by nasal tube feeding. Arch. Jap. Chir., **28**, 1356, 1958.
16) Nagase, M.: Experimental study on pathogenesis of acute postoperative pulmonary edema. Arch. Jap. Chir., **29**, 67, 1960.
17) Tamaki, A.: Influence of intravenous infusion of sesame oil emulsion on fluid distribution. Arch. Jap. Chir., **28**, 3028, 1959.
18) Brodie, B. B.: Use of N-acetyl 4-aminoantipyrine (NAAP) in measurement of total body water (18928). Proc. Soc. Exp. Biol. & Med., **11**, 794, 1951.
19) Brodie, B. B. and Axelrod, J.: The fate of aminopyrine (pyramidon) in man & method for the estimation of aminopyrine and its metabolism in biological material. J. Pharm. & Exp. Therap., **99**, 171, 1950.
20) Asano, S. et al.: Estimation of the volume of body fluid compartments with NAAP, mannitol and T-1824. Sogo-igaku, **11**, 19, 1951.
21) Gregersen, M. I. and Stewart, J. D.: Simultaneous determination of the plasma volume with T-1824, and the "available fluid" volume with sodium thiocyanate. Am. J. Physiol., **125**, 142, 1939.
22) Gamble, J. L.: Chemical anatomy, physiology and pathology of extracellular fluid. Harvard Univ. Cambridge, 1949.
23) Kodeki, K.: Studies on the water metabolism. J. Jap. Surg. Soc., **53**, 803, 1953.
24) Saito, M.: Clinical chemical examinations with spectrophotometer. Nanzando, 1952.
25) Sunahara, M.: On the extracellular fluid volume of healthy adults or patients who suffered from various disease. Tokyo Medical Journal, **56**, 617, 1942.
26) Sunahara, M.: Extracellular water volume and clinic. Saishin-igaku, **5**, 12, 1951.
27) Sunahara, M.: Construction of extracellular fluid. Nissin-igaku, **38**, 1, 1951.
28) Schwartz, I. L.: Measurement of extracellular fluid by means of constant infusion technique without collection of urine. Am. J. Physiol., **160**, 526, 1950.
29) Nickerson, M. and Thomas, J. J.: Renal excretion of thiocyanate. J. Lab. & Clin. Med., 1951.
30) Scheinberg, I. H. and Kowalski, H. J.: The binding of thiocyanate to albumin in normal human serum and defibrinated blood with reference to determination of "thiocyanate space" J. Clin. Invest., **29**, 475, 1950.
31) Gregersen, M. I.: An analysis of colorimetric method in relation to plasma volume determination. J. Lab. & Clin. Med., **23**, 423, 1938.
32) Chinard, F. P., Vasburgh, G. J. & Ennes, T.: Transcapillary exchange of water and other substances in certain organs of the dog. Am. J. Physiol., **183**, 221, 1955.
33) Nitsche, G. A. et al.: Determination of blood volume. Am. J. Clin. Path., **17**, 239, 1947.
34) Nagasu, K.: The measurement of blood volume with evansblue. Surgery, **12**, 566, 1950
35) Orishige et al.: On the experiences of determination of circulating blood volume with evans blue. Rinsho-geka, **5**, 531, 1950.
36) Nakanishi, N.: Experimental and theoretical studies on the measurement of circulating blood volume: Nippon-junkanki-gakushi, **15**, 1, 1951.
37) Chinard, F. P.: Transcapillary pulmonary exchange of water in the dog. Am. J. Physiol., **178**, 197, 1954.
38) Kanai, I.: Methods of clinical examination. Kanehara-shuppan, Ltd., 1954.
39) Kroh, A. und Nakazawa, F.: Beitraege zur Messung der Kolloidosmotischen Druckes in biologischen Fluessigkeiten. Biochem. Z., **188**, 241, 1827.
40) Farkas, G.: Zum Problem der Berechnung des kolloidosmotischen Druckes der Bluteiweisskoerper. Z. Exp. Med., **97**, 18, 1935.

41) Hayakawa, J.: On the serum colloid osmotic pressure in the patients of kidney disease. Nagoya Medical Journal, **68**, 580, 1954.
42) Nakazawa, F.: On the colloid osmotic pressure of blood. Clinic of Blood, **1**, 95.
43) Mori, K. and Kobayashi, H.: The practice of the methods of the paper electrophoresis. lst. Nanzando, 1954.
44) Shibata, S.: Entrance of clinical biochemistry. 2nd ed., Kinpodo, 1955.
45) Yoshimura, K.: The analysis of disturbances in the metabolism of water and electrolytes before and after surgery. Jour. Jap. Surg. Soc., **55**, 1237, 1955.
46) Takafuji, T.: The significance of electrolytes induced in the nourishing fluids. Recent Advances in Surgical Research, 2nd ed., 1857.
47) Mizukawa, G.: Clinical and experimental studies upon the fluid therapy in surgical patients. Jour. Jap. Surg. Soc., **56**, 283, 1955.
48) Bland, J. H.: Clinical recognition and management of disturbances of body fluids. 2nd ed., W. B. Saunders Co., Philadelphia, London, 1956.
49) Hikasa, Y., Asada, S., Zaitsu, A., Tsukada, A. and Nakata, K.: Studies on the intravenous administration of fat emulsion. Arch. Jap. Chir., **21**, 1, 1952.
50) Hikasa, Y., Kuyama, T. and Otani, S.: Clinical application of fat emulsion. Arch. Jap. Chir., **25**, 396, 1956.
51) Durum, E. L., Paul, M. M. and Smith, E. P. B.: Lipid, detection in paper electrophoresis. Science, **116**, 428, 1952.
52) Elaine, T., Bossack, Chun-Iwang and David, Adiersberg: Comparative studies of lipoprotein in various species by paper electrophoresis. Proc. Soc. Exp. Biol. & Med., **87**, 637, 1954.
53) Yamaguchi, M.: The ultrastructure of experimental acute pulmonary edema. (light and electron microscopic study). Arch. Jap. Chir., **29**, 482, 1960.
54) Shibusawa, K.: Abnormal metabolism of water and electrolytes due to surgical insult. Nippon-rinsho, **11**, 347, 1953.
55) Shibusawa, K.: Pituitary-adrenocortical-system due to surgical insult. Saishin-igaku, **7**, 1041, 1952.
56) Shibusawa, K.: Studies of antidiuretic substance in serum. Sogo-igaku, **10**, 304, 1953.
57) Shibusawa, K.: Hepato-renal syndrome. Rinsho, **7**, 649, 1952.
58) Shibusawa, K.: Vasodepressor material (VDM) due to liver. Saishin-igaku, **7**, 159, 1951.
59) Shibusawa, K.: Consideration of postoperative oliguria. Rinsho, **3**, 802, 1950.
60) Shibusawa, K.: Shock especially and hypotension. Operation, **6**, 356, 1952.
61) Shibusawa, K.: Shock in practice. Igaku-shoin Ltd., 1956.
62) Verney, E. B.: The antidiuretic hormon and the factors which determine its release. Proc. Roy. Soc. London, s. B., 135, 25, 1947.
63) Leaf, H. and Mamby, A. R.: An antiduretic mechanism not regulated by extracellular fluid tonicity. J. Clin. Invest., **31**, 60, 1952.
64) Matsuda, S.: Experimental study on the nutritional significance of fat from the view-point of its effects on the liver glycogen content. Arch. Jap. Chir., **28**, 3008, 1959.
65) Burr, G. O. and Burr, M. M.: A new deficiency disease produced by the rigid exclusion of fat from the diet. J. Biol. Chem., **82**, 203, 1929.
66) Deuel, H. J. Jr.: Nutritional significance of the fats. Progress in the chemistry of fats and other lipids. Volume 2, Pergamon Press, 1954.
67) Burr, G. O.: Significance of the essential fatty acids. Fed. Proc., **1**, 224, 1942.
68) Essential fatty acids. Butterworths Scientific Publications, 1958.
69) Jindo, A.: A micromethod for determining polyunsaturated fatty acids; its clinical and experimental applications. Arch. Jap. Chir., **30**, 1, 1961.
70) Deuel, H. J. Jr.: Nutritional significance of the fats. Progress in the chemistry of fats and other lipids. p. 100, Volume 2, Pergamon Press, 1954.
71) Tanaka, Y.: Unpublished.
72) Nakayama, K., Wakizaka, J., Sagawa, Y., Hayashi, K. and Yoshihara, Y.: Symposium on acute postoperative pulmonary edema. J. Jap. Thorac. Surg. Soc., **6**, 1, 1958.

73) Altschule, M. D.: Acute pulmonary edema. Grune & Stratton Publishers, 1954.
74) Henneman, P. H.: Acute pulmonary edema, with special reference to experimental studies. New England J. Med., **235**, 590, 619, 1946.
75) Belknap, E. L.: Acute pulmonary edema, endogenous and exogenous causes, with therapy. Diseases of chest, **20**, 630, 1951.
76) Reichsman, F.: Studies on the pathogenesis of pulmonary edema following bilateral vagotomy. Am. Heart J., **31**, 590, 1946.
77) Richters, C. P.: The physiology and cytology of pulmonary edema and pleural effusion produced in rats by alpha-naphthyl thiourea (ANTU). J. Thorac. Surg., **23**, 66, 1952.
78) Latta, H.: Pulmonary edema and pleural effusion produced by acute alphanaphthyl thiourea poisoning in rats and dogs. Bull. Johns Hopkins Hospital, **80**, 181, 1947.
79) Doyle, J. T., Wilson, J. S., Estates, E. H. & Warren, J. M.: The effect of intravenous infusions of physiologic solution on the pulmonary capillary pressure in man. J. Clin. Invest., **30**, 345, 1951.
80) Paine, R., Smith, J. R. Butcher, H. R. & Howard, F. A.: Heart failure and pulmonary edema produced by certain neurologic stimuli. Circulation, **5**, 759, 1952.
81) Robinson, J. R.: Reflections on renal function. Printed in Holland for Blackwell Scientific Publications, Ltd., 1954.
82) Yannet, H. & Darrow, D. G.: The effect of depletion of extracellular electrolytes on the clinical composition of skeletal muscle. J. Biol. Chem., **134**, 721, 1940.
83) Abbott, W. E.: The danger of admitting parenteral fluids by hypodermoclysis. Surgery, **32**, 305, 1952.
84) Tamaki, Y.: unpublished.
85) Kramár, J. and Levine, V. E.: Influence of fats and fatty acids on the capillaries. J. Nutrition, **50**, 149, 1953.
86) Kramár, J. and Simay-Kramár, M.: The effect of adrenalectomy, surgical trauma and ether anesthesia upon the capillary resistance of the albino rat. Endocrinology, **52**, 453, 1953.
87) Forsham, P. H. and Thorn, G. W.: The adrenals. Textbook of Endocrinology. W. B. Saunders, 1955.
88) Menkin, V.: Effect of adrenal cortex extract on capillary permeability. Am. J. Physiol., **129**, 691, 1940.
89) Sayers, G.: The adrenal cortex and homeostasis. Physiol. Reviews, **30**, 241, 1950.
90) Imagre, D. J. and Baker, B. L.: Physiological and therapeutic effects of corticotropin (ACTH) and cortisone. C. C. Thomas Springfield, U. S. A., pp. 172, 1953.
91) MacMillan, A.L. and Sinclair, H.M.: The structural function of essential fatty acids. Essential fatty acids. p. 208, Butterworths Scientific Publications, 1958.
92) Opsahl, J. C.: Role of certain steroids in adrenal hyaluronidase relationship. Yale J. Biol. & Med., **22**, 115, 1949.
93) Winter, C. A. and Flataker, L.: Influence of cortisone and related steroids upon spreading effect of hyaluronidase. Federation Proc., **9**, 137, 1950.

和 文 抄 録

不可欠脂酸欠乏時の体内水分代謝に関する研究

京都大学医学部外科学教室第2講座（指導：青柳安誠教授）

小 林 真 佐 夫

われわれの教室創製になる20%ゴマ油乳剤を用い，不可欠脂酸を充分に含有した脂質の投与が水分代謝にいかなる影響を及ぼすかを，まず健常成犬を用いて実験的に匡したる結果，次の結論に到達した．即ち，

(1) 手術前後に亘つて不可欠脂酸を充分に含有した脂質を投与すると，生体内水分分布を終始可及的正常状態近くに保持せしめ，たとい脱水や過剰給水が行なわれても，対照群のように正常範囲内から強く逸脱した異常な生体内水分分布を招来することがない．

(2) 不可欠脂酸を充分に含有した脂質とリンゲル氏液，5％ブドウ糖液を術前に併用投与すれば，術前の個体の脱水状態の改善に有効的に作用するが，このことは術前には患者を常に軽度の Overhydration の状態におくべきであるとする外科医のとるべき一般概念からしても，真にそれは合理的処置ということが出来る．

(3) 不可欠脂酸を充分に含有した脂質とリンゲル氏液，5％ブドウ糖液を術前術後を通じて続けて併用投与すると，術後の水分代謝も極めて順調で，術後の乏尿期に於ても体内の水分貯溜が極端に増大することなく，回復利尿の時期へと移行する．

(4) 術前術後に不可欠脂酸を充分に含有した脂質を投与すると，術後性ショックの防止に有効的に作用するようである．

(5) 不可欠脂酸を充分に含有した脂質投与の手術前後の水分代謝に及ぼす効果は，要するに，その投与によつて，終始血清蛋白濃度，血清アルブミン濃度が可及的正常状態近くに保たれて，その為に血清膠質滲透圧が有効的に保持されたものとも考えられるが，また同時に脂質中に豊富に含有されている不可欠脂酸の作用によつて，術前後を通じ，その個体の毛細血管あるいは細胞膜の水分透過性の異常亢進が充分に抑制された事実も大いに与つて力のあつたものと思考される．

併し以上の実験成績は何れも健常犬を使用してのものであつて，それを以て直ちに実際の臨床に於て取扱う各種病態下の患者の手術前後の水分代謝の様相と速断することは許されない．われわれ外科医の取扱う患者は，その一般通則として食餌摂取の障害あるいは癌腫の存在にもとずく悪液質等のために，その栄養状態は可成り低下していて，而もまた斯る患者ではその生体内不可欠脂酸の保有量も一般に低下しているから，斯る患者に手術が施され，且つ術後に過剰給水が行なわれた際には，その個体の生体内水分の分布状態はどのような態度を示すようになるかは極めて重要な問題である．

それで，われわれは更に不可欠脂酸欠乏犬を作製し，これに胃切除術を施すと同時に，その術前術後に亘つて単なる晶質の輸液を行なつた際と，同時に不可欠脂酸を充分に含有した脂質をも併せて投与した際に，当該個体が術後の過剰給水に対して体内水分代謝がいかなる反応を示すかをそれぞれ比較検討し，次の結論に到達した．即ち，

(1) 不可欠脂酸の欠乏した個体に手術侵襲を加える際には，その不可欠脂酸欠乏状態を是正しておくことが，水分代謝の面からみて非常に重要な処置である．

(2) 不可欠脂酸の欠乏した個体に対し，その欠乏を是正しておくことなく手術侵襲を加えると，術後の過剰給水によつて水分の体内異常蓄積を招き，而も細胞内液相の著しい拡大を来し，水中毒症や術後急性肺水腫を招来する怖れが大である．

(3) 不可欠脂酸の欠乏した個体に対しても，その術前術後に亘り充分な不可欠脂酸の補給を行ない乍ら手術を施行すれば，たとい術後の過剰給水が行なわれても，その際は細胞外液相の拡大のみに止まり，細胞内液相の拡大という状態まで発展することはない．従つて，水中毒症や術後急性肺水腫を来たす怖れがない．このような意味でも，生体内不可欠脂酸の欠乏を来たしていることの多い食餌摂取の障害あるいは癌腫の存在するような外科的手術患者に対し，術前術後の処置として良質な而も不可欠脂酸を充分に含有した脂質を補給することは忽せにすることが出来ない．

(4) 不可欠脂酸の欠乏した個体に於て，何故に著しい水分代謝の異常状態が惹起され易いか，これについては，次のような種々の機序が考えられる．即ち，不可欠脂酸の欠乏に際しては，当該個体の毛細血管壁及び細胞膜の透過性は平素から異常に亢進しているのみでなく，術後には，毛細血管や細胞膜の透過性に対して抑制的に作用する Glucocorticoids の分泌機能が Stress を契機として特に不可欠脂酸の欠乏した個体にあつては著しく低下し，また不可欠脂酸は Lipotropic substance としての作用を有し，更に術後の肝グリコーゲン保持に重要な役割を果しているから，それが欠乏すれば，肝機能の低下を介して術後の ADH 消却機能の減弱を招くようになり，斯くして術後乏尿の機序を益々助長する要因が相重なるようになるためであろう．